
Establishment of a normal hematopoietic and leukemia stem cell hierarchy.

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Scientific Abstract:

Many types of adult tissues, especially for high turnover tissues such as the blood and intestinal system, stand on a hierarchical tissue-specific stem cell system. Tissue-specific stem cells concurrently have self-renewal capacity and potential to give rise to all types of mature cells in their tissue. The differentiation process of the tissue-specific stem cell is successive restriction of these capacities. The first progeny of tissue-specific stem cells are multipotent progenitors (MPPs) that lose long-term self-renewal capacity yet have full lineage potential. MPPs in turn give rise to oligopotent progenitors, which then commit into lineage-restricted progenitors. This hierarchical system enables a lifelong supply of matured functional cells that generally have a short life span and a relatively high turnover rate. In this chapter, we review our findings and other key experiments that have led to the establishment of the current cellular stem and progenitor hierarchy in the blood-forming systems of mice and humans for both normal and leukemic hematopoiesis. We also review select signaling pathways intrinsic to normal hematopoietic and leukemic stem cell populations as well our recent findings elucidating the possible origin of the leukemia stem cell.

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